Abstract

The frequency of emerging disease is expected to grow as ongoing climate change and other anthropogenic effects drive new host and pathogen interactions. Shaping the outcomes of those interactions are the resident host microbiota. The microbiota have been shown to produce both reduced and enhanced virulence in hosts challenged by pathogens, depending on the context and organisms involved. In the context of emerging disease interactions, how the microbiota affects infection outcomes may be especially difficult to predict. As such, we investigated host gene expression to understand the molecular causes of microbiota-mediated enhanced virulence during novel pathogen invasion. We conducted transcriptomic analyses of *Caenorhabditis elegans* nematodes colonized by an ecologically relevant model microbiota community infected by the invasive bacterial pathogen, S*taphylococcus aureus*. We found microbiota and pathogen co-colonized hosts may become more susceptible to severe infection by changes in collagen biology mediated by the microbiota. Furthermore, microbiota colonized hosts increased expression of immunity genes and both increased (heat-shock) and decreased (unfolded protein) stress responses during infection, which could encompass both causes and effects of enhanced virulence. Taken together, our results indicate that molecular changes in the hosts mediated by a typically beneficial microbiota may incur significant costs when challenged by a novel invading pathogen.